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THE EFFECT OF UDMH INJECTION ON LEARNED BEHAVIOR IN THE JAVA MONKEY

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FOREWORD

This work was performed jointly by members of the 6571st Aeromedical Research Laboratory, Holloman Air Force Base, New Mexico, and the 6570th Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio, between September 1961 and February 1962. The research was conducted in support of Project 6302, "Toxic Hazards of Propellants and Materials," Task 630202, "Pharmacology and Biochemistry," for the Toxic Hazards Section, Physiology Branch, Biomedical Laboratory, 6570th Aerospace Medical Research Laboratories. The authors are indebted to Nelson DeLavan, Monnie Hedges, and Bob Hall, former Scientific Aides of the 6571st Aeromedical Research Laboratory, for their valuable assistance in the conduct of the experiments.

Animal experimentation reported herein was performed in accordance with "Principles of Laboratory Animal Care" established by the Institute of Laboratory Animal Resources, National Academy of Sciences.

ABSTRACT

Three experiments were conducted involving UDMH injection of the java monkey to study the effect of UDMH on performance of a learned task. The results of the three experiments indicated that a UDMH dosage of 30 mg/kg intraperitoneally is insufficient to produce significant changes in learned behavior.

PUBLICATION REVIEW

This technical documentary report has been reviewed and is approved.

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THE EFFECT OF UDMH ON LEARNED BEHAVIOR IN THE JAVA MONKEY

I. INTRODUCTION

In recent years, there has been a continuing interest in the toxicology and pharmacology of 1, 1-dimethylhydrazine (UDMH). This interest has evolved from the use of multiton quantities of UDMH as a propellant and the increased possibility of the hazards which it may thus impose for industrial and military personnel engaged in missile operations. Consequently, extensive effort has been expended toward the elucidation of the toxic manifestations of UDMH and the establishment of short-term tolerance criteria for the compound (Ref. 1, 2, 3, 4, 5, 6). In the studies just cited it has been demonstrated that UDMH toxicity is primarily associated with central nervous system (CNS) manifestations in the form of clonic-tonic convulsions and death. With the exception of emesis, no other clinical manifestations of toxicity have been noted until convulsions occur. Back et al. (Ref. 2) have determined the convulsive threshold in the java monkey to be approximately 40 mg/kg of body weight and the emetic threshold 30 mg/kg. With the exception of emesis, doses of 30 mg/kg of UDMH cause no apparent physiological impairment of either an acute or permanent nature. However, nothing was accomplished in their research regarding the effect of UDMH, of any dosage, on learned behavior in the java monkey. Therefore, it was felt that, although animals showed no physiological impairment, there might possibly be psychological effects.

Experiment I

The first experiment was designed to determine the effects of UDMH on java monkey performance of a Response-Shock (R-S) avoidance task which is described later.

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* Formerly Aeromedical Field Laboratory

II. METHOD

A. Subjects

The Ss were four male java monkeys (macaque cynomolgus) approximately three years of age. All Ss had been trained to a stabilized response rate on the task under investigation.

B. Apparatus

The Ss were restrained in chairs like the one shown in Figure 1, with a stimulus box and response lever located in the positions shown relative to the chair and the animal. The behavioral task was programmed with Foringer automatic operant equipment and response data were obtained by means of a Grason-Stadler print-out counter set to yield response data over the desired time interval. A Foringer shocking unit was programmed to deliver a 0.5-second shock of 520 volts at 5 milliamperes applied to the buttocks of a subject in the event the desired response did not occur within the time period specified. Electrical connections between the stimulus-box, response lever, and shock terminals were made through a hole in the ceiling of an isolation cubicle. Feces and urine were collected in a large plastic container located directly below the subject. The entire unit consisting of the restraint chair, stimulus box, response lever, and waste container was housed in the portable isolation cubicle with interior dimensions of 47 inches in length, 30 inches in width, and 57 inches in height. The outside wall of the cubicle is covered with acoustical tile and the inside wall is lined with galvanized metal. A "dead-air" space of two inches between these walls, together with the acoustical tile, provided for "deadening" of the interior to about a 45-decibel sound pressure level, as well as eliminating most environmental distractions. A 15-watt standard cool white fluorescent lamp provided illumination inside the cubicle. This light was kept on throughout all testing sessions.

C. Performance Task

A Response-Shock avoidance task was the dependent behavioral variable. The cue to a subject that the task was in effect was a red light located in the lower right quadrant of the stimulus box. The task required that a subject press on the lever mechanism at least once every 20 seconds in order to avoid shock. Each time the subject pressed the lever he

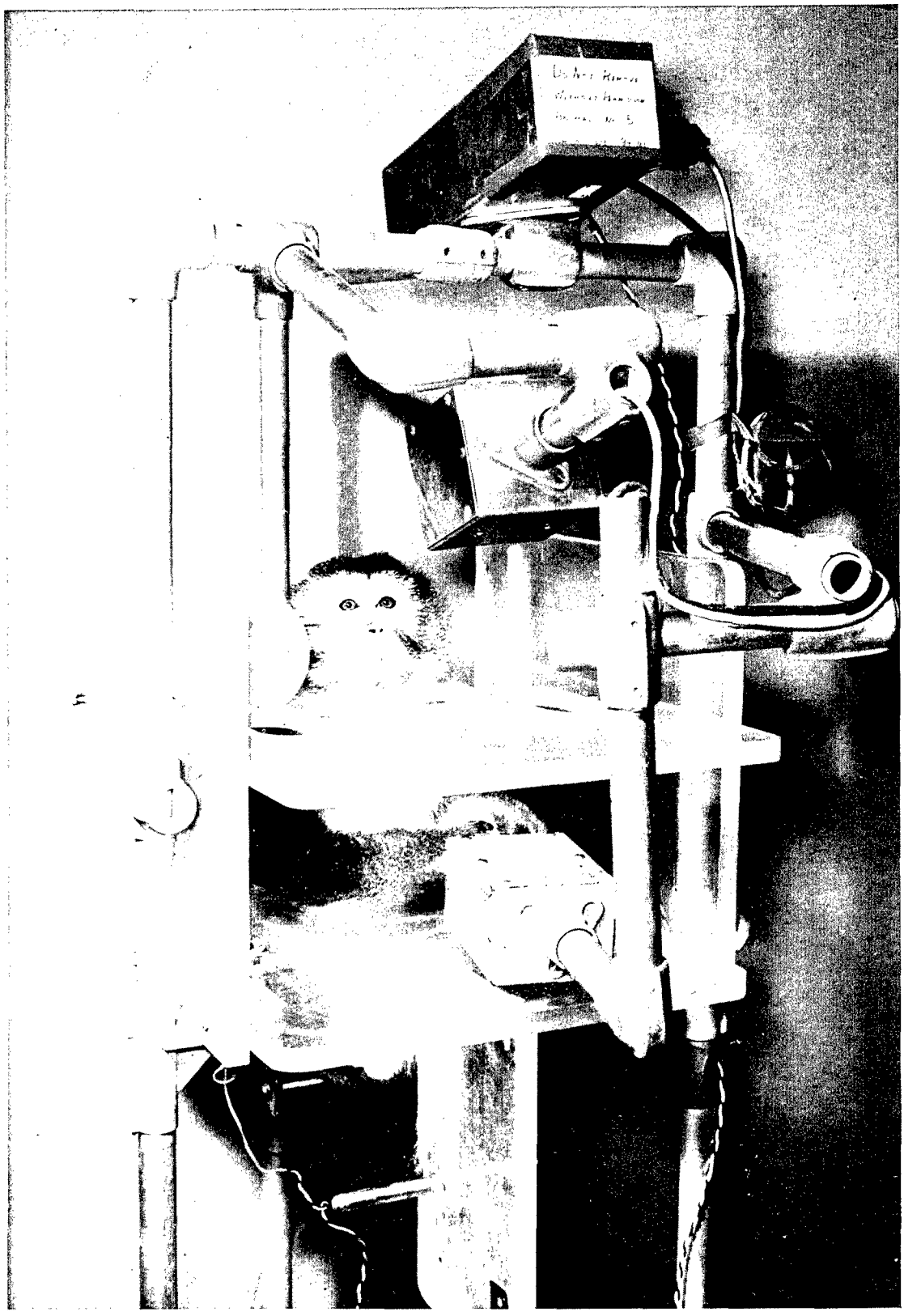

Figure 1. Restraint Chair with Stimulus-Response Apparatus

received a brief flash of white light from the upper left quadrant of the stimulus box as secondary reinforcement. If a subject failed to respond within the twenty-second time period allotted him, he was shocked every two seconds until a response was made (shock-shock interval) (Ref. 7).

D. Procedure

Beginning at 8:00 a.m. each day for five days prior to UDMH injection, the Ss performed on the behavioral task the first 15 minutes of each hour for a total of eight work sessions in order to establish a control level under non-drug conditions. On the basis of performance during this period, two of the four Ss were matched with the other two; Ss 1 and 4 were designated control animals while Ss 2 and 3 were designated as experimental animals. These designations permitted a comparison of changes in behavior on the part of the two groups as well as providing for each animal to act as his own control. Once these groups had been established the UDMH injection phase of the experiment began.

Control and experimental animals were injected interperitoneally (I. P.) in a random order at 7:40 a.m. The control animals were injected with 2 cc's of saline, while the experimental animals were injected with 30 mg/kg body weight of UDMH diluted with saline to 2 cc's total solution. At 8:00 a.m. all subjects were placed on the same work schedule as that outlined for the pre-UDMH phase of the experiment. Immediately following each 15-minute performance session, one cc of blood was drawn in random order from both control and experimental animals in order to assess UDMH content in the blood throughout the performance period.

E. Statistical Design

McNemar's Comparison of Change Statistic was employed (Ref. 8) to evaluate the "difference between the differences" of the control and experimental groups from the pre-UDMH performance phase to performance following UDMH injection. In addition, the change occurring for each animal was also examined. McNemar's statistic takes into account the correlation which exists when matching is performed or when repeated measures are made on the same subject.

III. RESULTS AND DISCUSSION

The statistical analysis yielded a t-ratio of 8.39 between the control and experimental groups which is significant beyond the .01 level (one-tail test). When each animal was considered as his own control the t-ratios for the two experimental animals were both significant beyond the .01 level, while the t-ratios for the two control animals were not significant. The performance of Ss during the pre-UDMH injection and UDMH injection phases of the experiment is presented in Figure 2. UDMH content in the blood of the two experimental animals agreed with previous findings and corroborated Back and Tamas' results in that the content could be read from the standard curve, with the recognition that readings from this low concentration are more difficult to accomplish (Ref. 1).

The results of this experiment led the investigators to hypothesize that a difference between the animals due to UDMH injection possibly did exist, but that a replication of the experiment was needed in order to increase the sample size and perhaps the reliability of the findings.

Experiment II

As indicated above, this experiment was accomplished in order to increase reliability by increasing the size of the sample. The investigators decided that blood samples would not be taken in this experiment because UDMH content in the blood during the first experiment was in good agreement with long-term findings.

The methods employed in this experiment were exactly the same as those for Experiment I, with the exception of blood sampling, and that control and experimental groups were reversed. This experiment followed the first by three weeks to allow for the elimination of any UDMH residue (Ref. 1).

IV. RESULTS AND DISCUSSION

The statistical analysis yielded a t-ratio between the control and experimental groups which was not significant (one-tail test). When each animal was considered as his own control the t-ratios were also insignificant. The performance of Ss during the pre-UDMH injection and UDMH injection phases of the experiment is presented in Figure 3. Obviously, these findings completely contradicted those of the first experiment. After some thought, the investigators hypothesized that, since in the

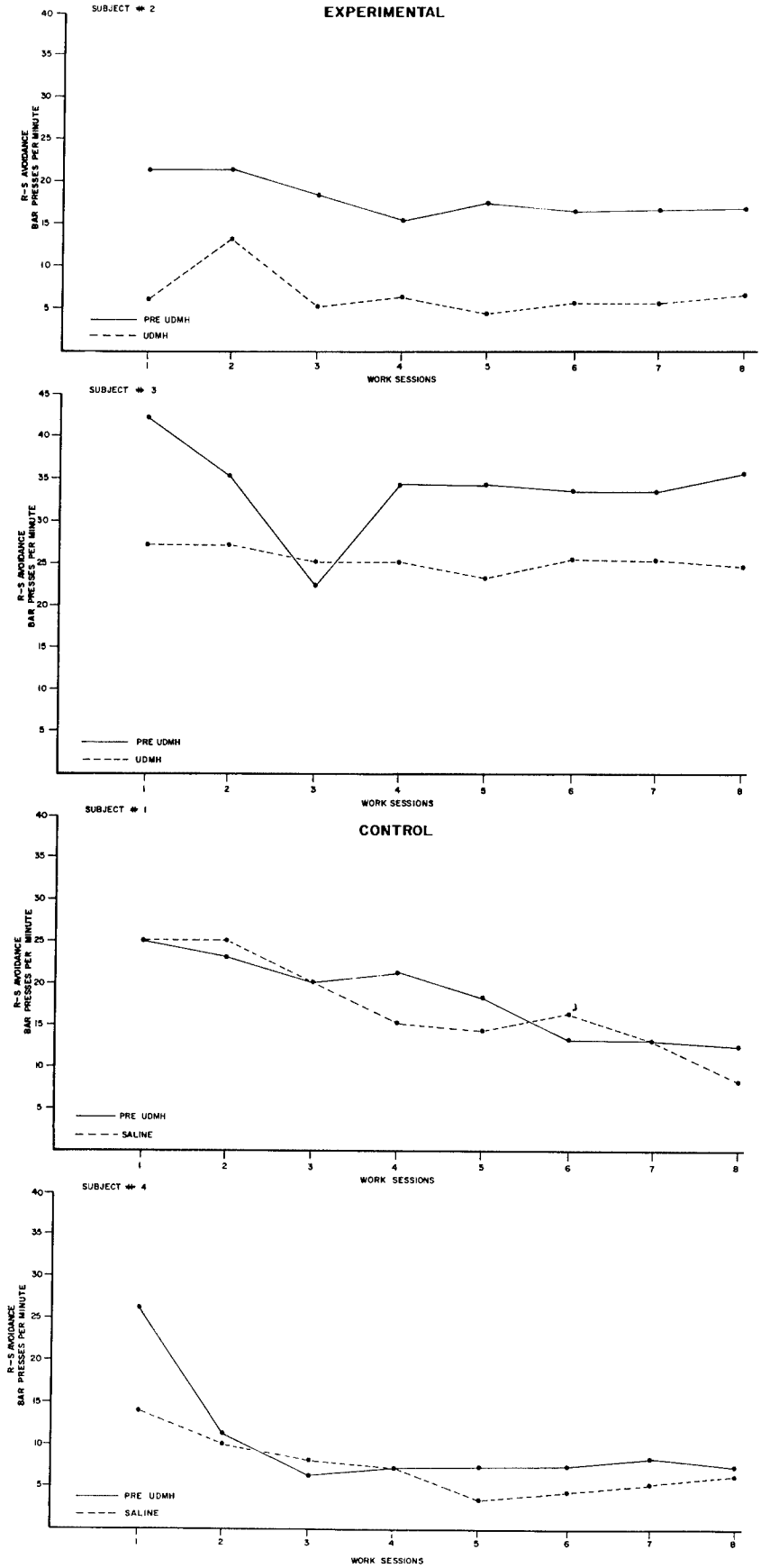

Figure 2. Performance of Experimental and Control Ss During Experiment I

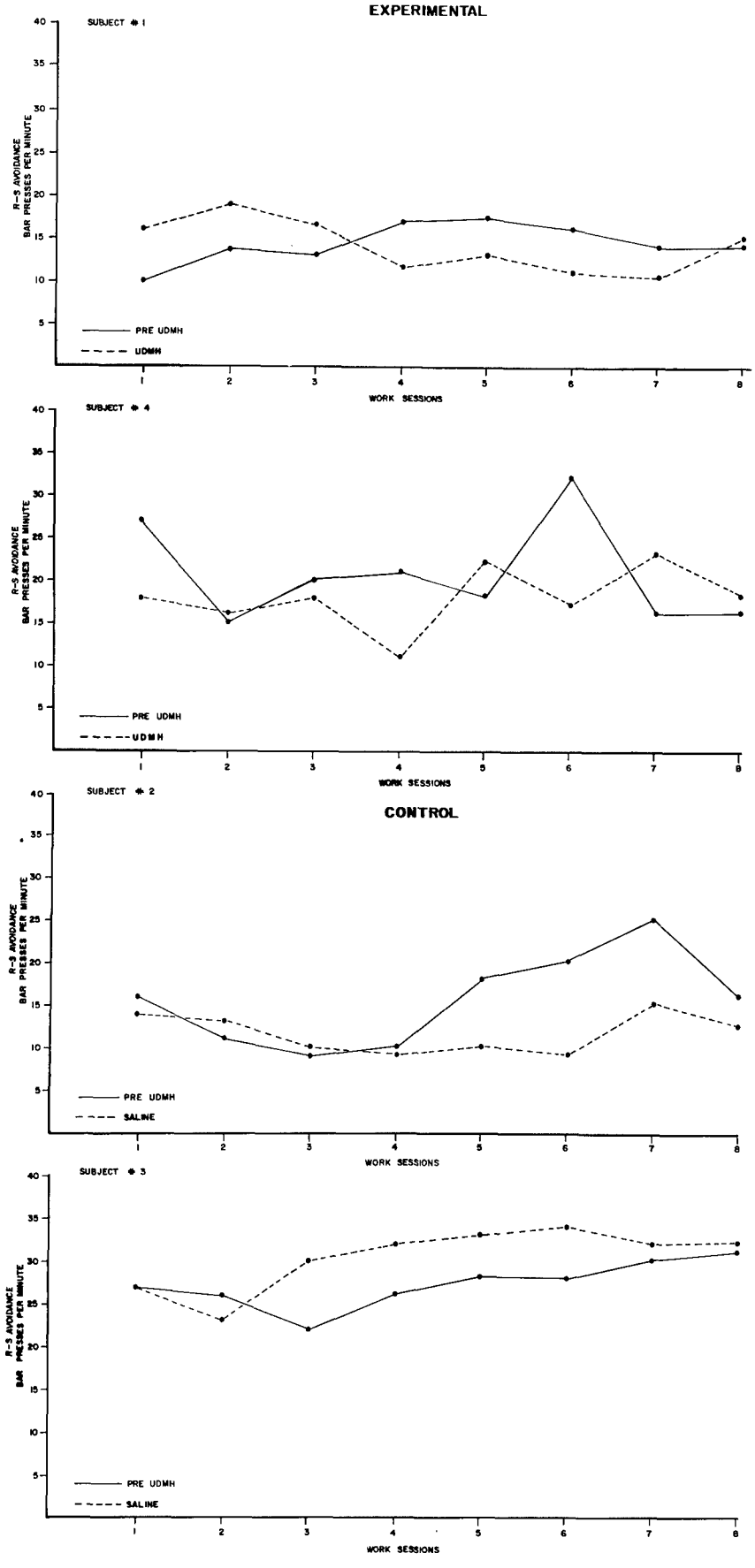

Figure 3. Performance of Experimental and Control Ss During Experiment II

first experiment both groups were sampled for blood and this was the only difference between the two experiments, an interaction between blood sampling and UDMH injection must have existed in great enough magnitude to produce a significant experimental effect. Since the performance of control animals in the first experiment did not change significantly, all evidence suggested that blood letting alone was not sufficient to produce a behavioral change. Further, it appeared that 30 mg/kg of UDMH alone might also be insufficient to bring about a change in behavior. Thus, a third experiment was accomplished.

Experiment III

This experiment was required because of the contradictory results obtained from the first two experiments.

The methods employed in this experiment were exactly the same as those for Experiment II in which blood sampling was omitted. However, seven Ss were employed in this experiment, including the four Ss used in the preceding experiments. Ss 1, 3, 4, and 6 were designated as experimental animals and Ss 2, 5, and 7 as control animals. A matched group statistical design was used, still employing McNemar's statistic. This experiment was accomplished approximately 60 days after Experiment II.

V. RESULTS AND DISCUSSION

The statistical analysis yielded a t-ratio between the control and experimental groups which was not significant (one-tail test). When each animal was considered as his own control, six of the seven t-ratios were also insignificant; one of the experimental animals showed a decrement in performance significant at the .05 level. The performance of Ss during the pre-UDMH and UDMH injection phases of the experiment is presented in Figure 4.

VI. CONCLUSIONS

The results of Experiment III, along with those of Experiment II, led the investigators to conclude that a UDMH dosage of 30 mg/kg is insufficient to produce significant changes in learned behavior (R-S avoidance); however, the continued study of UDMH is imperative.

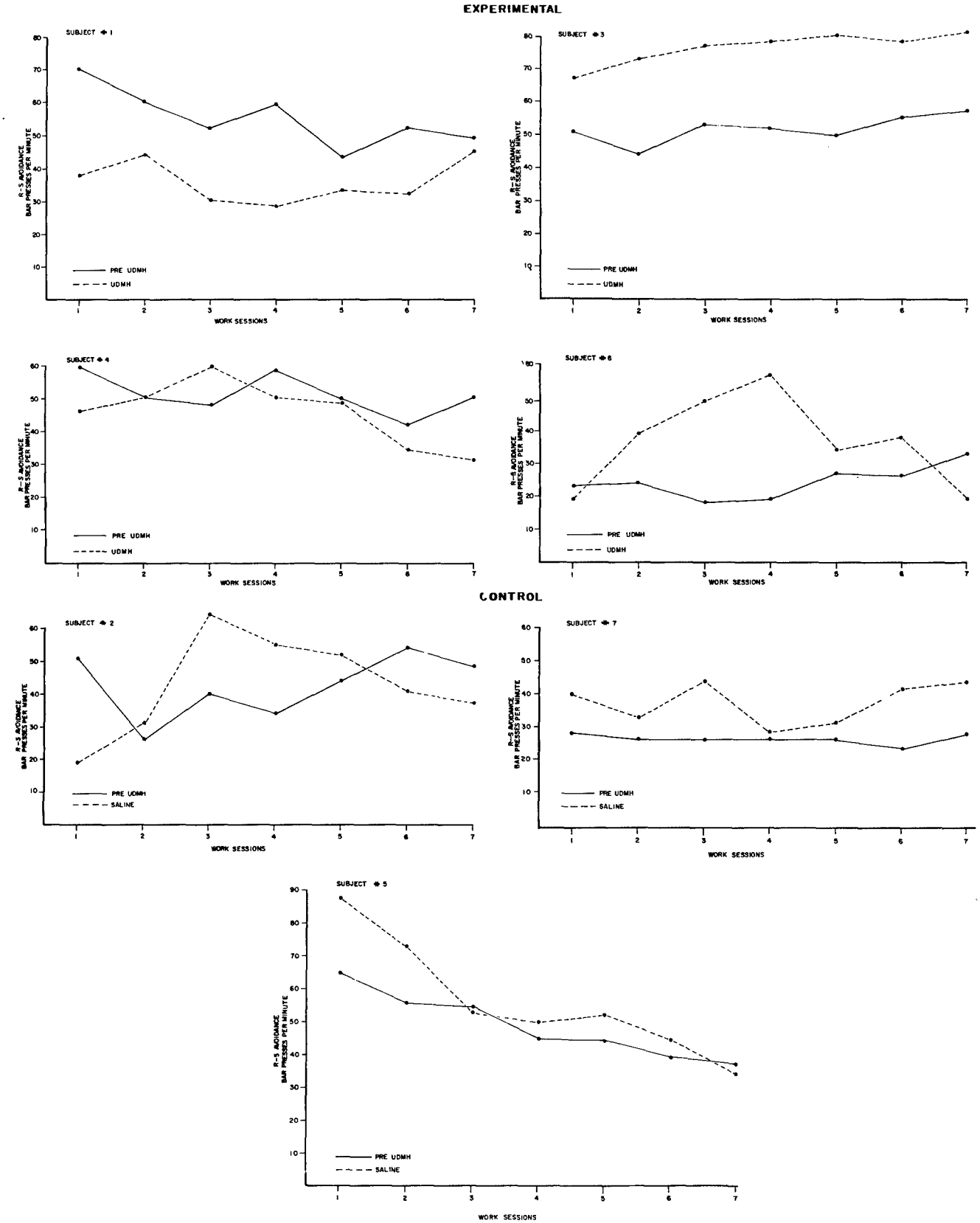

Figure 4. Performance of Experimental and Control Ss During Experiment III

Greater information regarding the effect of UDMH on behavior is needed and is more likely to be gained from experiments employing a larger number of subjects, different dosages of UDMH, and varied work periods. Complex factorial designs with several replications per condition will probably prove to be of greatest benefit; therefore, future experiments by these investigators will proceed along such lines.

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Unclassified report

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